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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/533,547	03/23/2000	Randall S. Kent	JAO 28796.02	3851

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EXAMINER
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MCKANE, ELIZABETH L

ART UNIT	PAPER NUMBER
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1744

16

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/533,547

Applicant(s)

KENT ET AL.

Examiner

Leigh McKane

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 3/21/3003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-28,30 and 34-172 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-28,30 and 34-172 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

*Claim Rejections - 35 USC § 103*

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1, 2, 4-6, 11-18, 20-22, and 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakai et al ("Microbiological Studies on Drugs and Their Raw Materials") in view of Hackett et al (WO 91/16060).

Sakai et al teaches the sterilization of enzymes containing glucose and/or lactose (food ingredients) and L-cysteine, an anti-oxidant protectant. The enzyme preparations are sterilized in lyophilized form with gamma radiation at a dose rate of 3.45 rad/hr (0.345 kGy/hr). Enzymes are a proteinaceous material and both glucose and lactose are both carbohydrates. See pages 1130-1131. Sakai et al fails to disclose adding a sensitizer to the biological material before irradiation.

Hackett et al teaches sterilizing biological material wherein a sensitizer may be added before irradiation with gamma radiation. See page 15, lines 22-33. As Hackett et al discloses that sensitizers bind to microbial DNA and/or RNA and generate hydroxyl radicals upon radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the enzymes in the method of Sakai et al, in order to increase radiation effectiveness.

Sakai et al teaches generally the sterilization of "biological materials" and specifically

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teaches the sterilization of an enzyme, trypsin. Although trypsin is not a component of blood, blood does contain other enzymes. Thus, it would have been obvious to one of ordinary skill in the art to use the method of Sakai et al to sterilize other enzymes and biological materials since the method has been shown to be effective and since Sakai et al discloses that "the biological activities of these drugs are not impaired and undesirable byproducts are not formed."

3. Claims 1, 2, 4-8, 14, 19, 21, 22, and 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chanderkar et al ("The Involvement of Aromatic Amino Acids in Biological Activity of Bovine Fibrinogen as Assessed by Gamma-Irradiation") in view of Hackett et al.

Chanderkar et al teaches sterilization of fibrinogen in lyophilized form. The preparation is irradiated by gamma radiation with a dose rate of 12,500 R/min (7.5 kGy/hr). Potassium iodide, an electron scavenger, is added as a protectant. See pages 283-284. Chanderkar et al fails to disclose adding a sensitizer to the biological material before irradiation.

Hackett et al teaches sterilizing biological material wherein a sensitizer may be added before irradiation with gamma radiation. See page 15, lines 22-33. As Hackett et al discloses that sensitizers bind to microbial DNA and/or RNA and generate hydroxyl radicals upon radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the fibrinogen in the method of Chanderkar et al, in order to increase radiation effectiveness.

4. Claims 1, 2, 4-6, 9, 14, 18, and 20-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baquey et al ("Radiosterilization of albuminated polyester prostheses") in view of Hackett et al.

Baquey et al teaches the use of gamma radiation to sterilize albumin coated upon

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polyester. The samples were lyophilized and irradiated at a dose rate of 2600 rad/min (1.56 kGy/hr) in a low oxygen atmosphere (nitrogen). See page 186. Baquey et al is silent with respect to adding a sensitizer to the biological material before irradiation.

Hackett et al teaches sterilizing biological material wherein a sensitizer may be added before irradiation with gamma radiation. See page 15, lines 22-33. As Hackett et al discloses that sensitizers bind to microbial DNA and/or RNA and generate hydroxyl radicals upon radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the albumin in the method of Baquey et al, in order to increase radiation effectiveness.

In order to achieve a low oxygen atmosphere, Baquey et al uses an inert gas nitrogen. Although Baquey et al doesn't disclose argon as the inert gas, it is deemed obvious to substitute one inert gas for another in the method of Baquey et al.

5. Claims 1, 2, 5, 10, 14, 19, 22, and 25-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Field et al ("Susceptibility of Scrapie Agent to Ionizing Radiation") in view of Hackett et al.

Field et al teaches the sterilization of brain tissue that has been lyophilized. The tissue is irradiated with gamma radiation at a dose rate of 43,000 rad/min (25.8 kGy/hr). Field et al fails to disclose adding a sensitizer to the biological material before irradiation.

Hackett et al teaches sterilizing biological material wherein a sensitizer may be added before irradiation with gamma radiation. See page 15, lines 22-33. As Hackett et al discloses that sensitizers bind to microbial DNA and/or RNA and generate hydroxyl radicals upon radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the brain tissue in the method of Field et al, in order to increase radiation effectiveness.

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6. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sakai et al or Chanderkar et al or Field et al, all in view of Hackett et al as applied to claim 1 above, and further in view of Horowitz et al (U.S. Patent No. 5,981,163).

The references *supra* teach lyophilization of the product, but do not teach that the solvent removed is an organic solvent. Horowitz et al, however, teaches that it is known in the art to combine a radiation sterilization step with another sterilization step such as treatment with an organic (lipid) solvent. See col.7, line 66 to col:8, line 7. Since it would have been obvious to first treat the product with a lipid solvent to inactivate viruses, it would have been further obvious to remove the solvent before irradiation, in the manner of Sakai et al, Chanderkar et al, or Field et al.

7. Claims 30, 34-38, 43-50, 52-54, 57-61, 65-73, 75-77, 80-88, 92-100, 102-104, 107-116, 120-128, 130-132, 135-139, 141-147, 152-159, 161-163, 166-170, and 172 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakai et al in view of Horowitz et al.

Sakai et al teaches the sterilization of enzymes containing glucose and/or lactose (food ingredients) and L-cysteine, an anti-oxidant protectant. The enzyme preparations are sterilized in lyophilized form with gamma radiation at a dose rate of 3.45 rad/hr (0.345 kGy/hr). Enzymes are a proteinaceous material and both glucose and lactose are both carbohydrates. See pages 1130-1131. The stabilizer employed by Sakai et al is not the same as that claimed by the instant invention.

Horowitz et al discloses the use of an irradiation stabilizer, selected from polyhydric alcohols, rutin, glutathione, and others. See col.7, lines 1-7. As Horowitz et al teaches their use in the sterilization of sensitive biological materials with gamma radiation and discloses that these

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stabilizers are effective in reacting with both free radicals and reactive forms of oxygen, it would have been obvious to add use stabilizer of Horowitz et al in place of that of Sakai et al, which is only an anti-oxidant.

Sakai et al teaches generally the sterilization of "biological materials" and specifically teaches the sterilization of an enzyme, trypsin. Although trypsin is not a component of blood, blood does contain other enzymes. Thus, it would have been obvious to one of ordinary skill in the art to use the method of Sakai et al to sterilize other enzymes and biological materials since the method has been shown to be effective and since Sakai et al discloses that "the biological activities of these drugs are not impaired and undesirable byproducts are not formed."

Sakai et al teaches lyophilization of the product, but does not teach that the solvent removed is an organic solvent. Horowitz et al, however, teaches that it is known in the art to combine a radiation sterilization step with another sterilization step such as treatment with an organic (lipid) solvent. See col.7, line 66 to col.8, line 7. Since it would have been obvious to first treat the product with a lipid solvent to inactivate viruses, it would have been further obvious to remove the solvent before irradiation, in the manner of Sakai et al.

Sakai et al fails to disclose adding a sensitizer to the biological material before irradiation. Horowitz et al teaches sterilizing biological material wherein a sensitizer may be added before irradiation with gamma radiation. See col.7, lines 47-65. As Horowitz et al discloses that sensitizers improve radiation effectiveness by making microorganisms more susceptible to the radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the enzymes in the method of Sakai et al, in order to increase sterilization effectiveness.

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8. Claims 30, 34-40, 46, 48, 49, 51, 53, 54, 57-63, 69, 71, 72, 74, 76, 77, 80-90, 96, 98, 99, 101, 103, 104, 107-118, 124, 126, 127, 129, 131, 132, 135-138, 140, 149, 155, 157, 158, 160, 162, 163, 166-169, 171, and 172 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chanderkar et al in view of Horowitz et al.

Chanderkar et al teaches sterilization of fibrinogen in lyophilized form. The preparation is irradiated by gamma radiation with a dose rate of 12,500 R/min (7.5 kGy/hr). Potassium iodide, an electron scavenger, is added as a protectant. See pages 283-284. The stabilizer employed by Chanderkar et al (potassium iodide) is not the same as that claimed by the instant invention.

Horowitz et al discloses the use of an irradiation stabilizer, selected from polyhydric alcohols, rutin, glutathione, and others. See col.7, lines 1-7. As Horowitz et al teaches their use in the sterilization of sensitive biological materials with gamma radiation and discloses that these stabilizers are effective in reacting with both free radicals and reactive forms of oxygen, it would have been obvious to add use stabilizer of Horowitz et al in place of that of Chanderkar et al.

Chanderkar et al teaches lyophilization of the product, but does not teach that the solvent removed is an organic solvent. Horowitz et al, however, teaches that it is known in the art to combine a radiation sterilization step with another sterilization step such as treatment with an organic (lipid) solvent. See col.7, line 66 to col.8, line 7. Since it would have been obvious to first treat the product with a lipid solvent to inactivate viruses, it would have been further obvious to remove the solvent before irradiation, in the manner of Chanderkar et al.

Chanderkar et al fails to disclose adding a sensitizer to the biological material before irradiation. Horowitz et al teaches sterilizing biological material wherein a sensitizer may be



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added before irradiation with gamma radiation. See col.7, lines 47-65. As Horowitz et al discloses that sensitizers improve radiation effectiveness by making microorganisms more susceptible to the radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the fibrinogen in the method of Chanderkar et al, in order to increase sterilization effectiveness.

9. Claims 30, 34-38, 41, 46, 48-50, 52-56, 58-61, 64, 69, 71-73, 75-88, 91, 96, 98-100, 102-113, 119, 124, 126-128, 130-138, 141-144, 150, 155, 157-159, 161-169, and 172 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baquey et al in view of Horowitz et al.

Baquey et al teaches the use of gamma radiation to sterilize albumin coated upon polyester. The samples were lyophilized and irradiated at a dose rate of 2600 rad/min (1.56 kGy/hr) in a low oxygen atmosphere (nitrogen). See page 186. Baquey et al fails to disclose using a stabilizer.

Horowitz et al discloses the use of an irradiation stabilizer, selected from polyhydric alcohols, rutin, glutathione, and others. See col.7, lines 1-7. As Horowitz et al teaches their use in the sterilization of sensitive biological materials with gamma radiation and discloses that these stabilizers are effective in reacting with both free radicals and reactive forms of oxygen, it would have been obvious to add use stabilizer of Horowitz et al in the method of Baquey et al.

Baquey et al teaches lyophilization of the product, but does not teach that the solvent removed is an organic solvent. Horowitz et al, however, teaches that it is known in the art to combine a radiation sterilization step with another sterilization step such as treatment with an organic (lipid) solvent. See col.7, line 66 to col.8, line 7. Since it would have been obvious to

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first treat the product with a lipid solvent to inactivate viruses, it would have been further obvious to remove the solvent before irradiation, in the manner of Baquey et al.

Baquey et al fails to disclose adding a sensitizer to the biological material before irradiation. Horowitz et al teaches sterilizing biological materials wherein a sensitizer may be added before irradiation with gamma radiation. See col.7, lines 47-65. As Horowitz et al discloses that sensitizers improve radiation effectiveness by making microorganisms more susceptible to the radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the albumin in the method of Baquey et al, in order to increase sterilization effectiveness.

In order to achieve a low oxygen atmosphere, Baquey et al uses an inert gas nitrogen. Although Baquey et al doesn't disclose argon as the inert gas, it is deemed obvious to substitute one inert gas for another in the method of Baquey et al.

10. Claims 30, 34, 35, 37, 42, 46, 48, 49, 51, 57, 58, 60, 65, 69, 71, 72, 74, 77, 80-85, 87, 92, 96, 98, 99, 101, 104, 107-113, 120, 124, 126, 127, 129, 132, 135-138, 141-144, 151, 155, 157, 158, 160, 163, 166-169, and 172 are rejected under 35 U.S.C. 103(a) as being unpatentable over Field et al in view of Horowitz et al.

Field et al teaches the sterilization of brain tissue that has been lyophilized. The tissue is irradiated with gamma radiation at a dose rate of 43,000 rad/min (25.8 kGy/hr). Field et al fails to disclose using a stabilizer.

Horowitz et al discloses the use of an irradiation stabilizer, selected from polyhydric alcohols, rutin, glutathione, and others. See col.7, lines 1-7. As Horowitz et al teaches their use in the sterilization of sensitive biological materials with gamma radiation and discloses that these

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stabilizers are effective in reacting with both free radicals and reactive forms of oxygen, it would have been obvious to add use the stabilizer of Horowitz et al in the method of Field et al.

Field et al teaches lyophilization of the product, but does not teach that the solvent removed is an organic solvent. Horowitz et al, however, teaches that it is known in the art to combine a radiation sterilization step with another sterilization step such as treatment with an organic (lipid) solvent. See col.7, line 66 to col.8, line 7. Since it would have been obvious to first treat the product with a lipid solvent to inactivate viruses, it would have been further obvious to remove the solvent before irradiation, in the manner of Field et al.

Field et al fails to disclose adding a sensitizer to the biological material before irradiation. Horowitz et al teaches sterilizing biological materials wherein a sensitizer may be added before irradiation with gamma radiation. See col.7, lines 47-65. As Horowitz et al discloses that sensitizers improve radiation effectiveness by making microorganisms more susceptible to the radiation, it would have been obvious to one of ordinary skill in the art to add a sensitizer to the albumin in the method of Field et al, in order to increase sterilization effectiveness.

### ***Response to Arguments***

11. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.


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*Conclusion*

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh McKane whose telephone number is 703-305-3387. The examiner can normally be reached on Monday-Wednesday (7:15 am-4:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 703-308-2920. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9310 for regular communications and 703-872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.

  
**Leigh McKane**  
**Primary Examiner**  
**Art Unit 1744**

elm  
June 27, 2003